spindle, stellate and endothelial cells. Davis felt that the histological diagnosis was unquestionably syphilis.

SUMMARY. 1. Gummatous syphilis of the thyroid gland is of rare occurrence.

2. Women are more frequently the subjects than men.

3. The cases so closely resemble carcinoma clinically that a differential diagnosis on these grounds alone is often impossible.

4. The usual change is a hard, nodular or smooth tumor involving either lobe, the isthmus or the whole gland.

5. Symptoms due to thyroid disturbance are unusual, and when they occur are those of myxedema, or apparently rarely those of hyperthyroidism. Symptoms due to interference with respiration are very common, and may be so severe as to cause death.

6. If the patient is seen before death is imminent and antisyphilitic treatment instituted the prognosis is very good.

I wish to express my appreciation to Prof. Udo J. Wile for the privilege of reporting this case and for his invaluable criticism.

THE DIFFERENTIAL DIAGNOSIS OF AFFECTIONS OF THE RIGHT UPPER QUADRANT.*

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THE differential diagnosis of affections of the right upper quadrant resolves itself into an interpretation of the various forms of "dyspepsia." Dyspepsia, however, is such a protean condition and arises from so many widely divergent causes that its translation into clinical entities is usually difficult. In the phylogenetic development of the gut tube there has come about a radical subdivision in morphology, physiology and function, and the stomach gives forth reflex symptoms from a variety of diseased organs more or less remotely situated.

In an analysis of indigestion we find that approximately 40 per cent. are due to disease within the abdomen but arising from other organs than the stomach: that 40 per cent. are due to causes entirely without the abdomen and that only in 20 per cent. is there organic disease of the stomach.

Vander Hoof[1] analyzed the cause of indigestion in 1000 cases and found that appendicitis was the causal factor in approximately 25 per cent., cholecystitis in 10 per cent., peptic ulcer in 10 per cent., neurosis in 10 per cent., cancer in 5 per cent., visceroptosis, intestinal stasis in 10 per cent., while miscellaneous affections of the kidneys, lungs, eyes, etc., constituted approximately 30 per cent. It is a sad diagnostic commentary when 97 out of 1000 tabetics have had a laparotomy for a supposed intra-abdominal lesion,[2] 19 for gastric ulcer, 19 for gall-stones, 18 for appendicitis and 13 for salpingitis, etc.

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Cabot[3 4] found from a study of 1000 autopsies at the Massachusetts General Hospital and a comparison with the clinical findings that in gastric cancer a correct diagnosis was made in 72 per cent. In peptic ulcer, including both gastric and duodenal, a correct diagnosis was arrived at in only 26 per cent.

The very marked advance in the technical efficiency of roentgen diagnosis in the last few years shows how rapid has been our diagnostic progress with 67 per cent. correct diagnosis in duodenal ulcer and 80 per cent. correct diagnosis in gastric ulcer,[5] while 95 per cent. of gastric carcinoma are diagnosticated by this means.[6]

For all ordinary purposes of diagnosis we rely upon the history which still remains the keystone in the diagnostic arch of affections of the right upper quadrant. Clinically our problem is to differentiate gastroduodenal ulceration, gastric carcinoma, disease of the biliary apparatus, including pancreatitis, appendicitis and to a lesser extent lesions of the kidney and colon.

If we conceive the stomach as exercising properly two main functions, that of motion and secretion, we would reasonably expect that any ulcerative condition in the beginning before active infiltrative changes had occurred would manifest itself by aberrations either in the motor or secretory functions of the stomach. Is there anything distinct in the evolution of gall-bladder disease that demarks it from the evolution of peptic ulcer? Is there anything in the history of chronic appendicitis wherein it differs in sufficient degree to enable us to differentiate reflex gastric distress of appendicular origin from dyspepsia of gastroduodenal ulcer? We believe that the single factor of greatest importance in differential diagnosis is a carefully taken history. The history should be a citation of the facts of the disease from its beginning and in the order of their occurrence, and if properly taken should provide a means of making a clinical diagnosis. By clinical diagnosis we mean that the nature of the pathological process is determined with relative anatomical localization. It is obvious that one of the most prominent factors in the diagnosis of affections of the right upper quadrant is the correct interpretation of the discomfort and pain for which a patient usually consults a doctor. There are certain fundamental characteristics of abdominal pain—its onset, localization, point of election, maximum point of tenderness and the various paths of radiation and reflexion which are of great value in diagnosis, for within their group most of the affections that we must differentiate run true to type. First, let us take up the consideration of affections of the biliary tract. We prefer to use this generic designation rather than gall-stones, for gall-stones are an incident dependent upon the virulence of the infection. The gall-bladder, the liver, the pancreas and the stomach are embryologically, anatomically, physiologically and pathologically closely related, and should be considered as one physiological system.[7] Infection is the pathological activator of disease of the biliary apparatus, and while it is true that a gall-bladder may be sterile and yet contain stones, infection must have been present at the time the calculi were originally formed. In disease of the gall-bladder only approximately 75 per cent. are associated with stone, the other 25 per cent. represent varying degrees of infection not associated with the formation of calculi. Irrespective of the presence of calculi in disease of the gall-bladder the histories of a large number of cases will be found to present a composite picture in which four well-defined pathological stages are evidenced and which clinically may be translated into four sequential clinical pictures: (1) When the disease is confined to the gall-bladder; (2) when there are attacks of biliary colic; (3) when calculous obstruction to the common duct intervenes with jaundice; (4) when as a result of infection or trauma to the common duct there is an associated or coincident disease of the pancreas.

The early symptoms of gall-bladder disease are vague atypical symptoms of a qualitative dyspepsia. This dyspepsia conforms to no rule, exhibits no periodicity in its onset, and is characterized by variations in the degree of gas production, eructations, sense of fulness and weight or oppression with occasionally tenderness along the right costal margin. There is a characteristic chilly or goose-skin sensation after dinner and occasionally a slight catch in the breath, particularly on the right side, suggesting a pleurisy. This gastric irritability is made worse by greases, fried foods, apples, cheese and gas-producing carbohydrates in general. Occasionally there is an entire cessation of this indigestion, with prolonged periods of comparative gastric relief. After a variable period of time there is introduced into this picture an acute attack of pain, colicky in type, with marked predilection for nocturnal occurrence, and lasting four to six hours, and usually so severe as to require a hypodermic of morphin. This colic comes on without premonition or warning, although there is occasionally a suggestion of an aura in an unusual state of well-being.[8] Its marked and distinct characteristic is that it is of maximum intensity, occurs spontaneously, like lightning, has a short duration, disappears spontaneously, leaving a residual soreness along the right costal margin. The third clinical picture is due to calculous obstruction of the common duct and introduces for the first time the presence of jaundice. There may be a preceding history of gastric distress, interrupted by periods of colic and during one of these attacks of pain there is a sudden onset of jaundice which reaches a maximum intensity in twenty-four to forty-eight hours, and is associated with a febrile reaction usually so distinct as to suggest a malarial paroxysm with its chill, fever and sweat. This febrile reaction is so short as to give a characteristic intermittent or remittent fever variously described as "steeple-chart" temperature,[9] or the angle of cholangitic infection.[10] When we have a colic associated with jaundice and marked by fever, leukocytosis, etc., and occurring in that order we are warranted in making the diagnosis of calculous disease of the common bile duct.

It must not be forgotten that a calculus which is capable of passing through the cystic duct may pass throughout the common duct into the duodenum without producing any further trouble. There is, however, a great tendency for a stone in the common duct to become lodged at the ampulla of Vater and by accretions of pigment to increase quite rapidly in size. Whether from the presence of stone or the infection or both[11] it was early observed that there was a very marked association between affections of the biliary tract and pancreatitis.[12]

It is interesting to recall that in reporting the statistics of the Mayo Clinic[13] it was found that in 2611 operations on the gall-bladder the pancreas was involved in 7.6 per cent. In 325 operations on the common duct the pancreas was involved in 22 per cent. and in 168 operations for disease of the pancreas 81 per cent. were accompanied by or due to gall-stones. A number of men, Archibald,[14] particularly, have gone so far as to claim chronic pancreatitis is a common abdominal complaint and capable of diagnosis. "Given a case with acute abdominal pain referred chiefly to the upper half of the abdomen, if upon examination one finds the greatest tenderness located in the epigastrium about midway between the umbilicus and the ensiform cartilage, extending perhaps 1 inch or 1½ inches to the right, and in particular a similar distance to the left also, while absent over the gall-bladder region, if further in the history there are absent symptoms of gastric or duodenal ulcer, and there is no evidence of intestinal obstruction, then this case is in all probability one of pancreatitis."[14]

The clinical differentiation of acute pancreatitis is sometimes difficult and the description of Fitz[15] is even today the best epitome upon its diagnosis. "Acute pancreatitis begins with intense pain, especially in the upper abdomen, soon followed by vomiting, that is likely to be more or less obstinate, and not infrequently slight epigastric swelling and tenderness, accompanied with obstinate constipation. A normal or subnormal temperature may be present and symptoms of collapse precede by a few hours death, which is most likely to occur between the second and fourth day."

The history of pancreatic or biliary carcinoma is distinct. The genesis of tumors requires time and the history of the onset of jaundice is succinct and characteristic. By slow growth a neoplasm produces from day to day only minimal changes, whereas vascular or inflammatory processes produce extensive changes within a short time. Neoplasms of the biliary apparatus, the pancreas or the contiguous portion of the duodenum early invade or compress the termination of the bile and pancreatic ducts. Jaundice develops imperceptibly and without pain, so that from day to day it seems hardly to advance in intensity, but without pause or hesitation, without intermitting or remitting, it progressively deepens in intensity from mild to severe, from lemon to black, until it becomes the typical icterus melas. Its evolution is not associated with colic and in its earlier stages is usually devoid of pain. It is not associated with chills, fever or sweats nor leukocytosis. With such a history, malignancy is the probable diagnosis, and when this history is associated with a palpable or distended gall-bladder the diagnosis is almost positive. One of the few diagnostic laws that has stood the acid test is Courvoirsier's law. Courvoirsier enunciated his law: "In cases of chronic jaundice, due to blocking of the common duct, a contraction of the gall-bladder signifies that the obstruction is due to stone: A dilatation of the gall-bladder, that the obstruction is due to causes other than stone."[16]

In reporting the cases of the Massachusetts General Hospital, Cabot[17] found that "in 86 cases of obstruction of the common duct 57 were due to calculous obstruction and in 47 the gall-bladder was atrophied, in 8 it was normal and in 2 enlarged. In 29 cases the obstruction was due to causes other than stone. In 27 the gall-bladder was diseased and in 1 the gall-bladder was empty and in 1 contracted around the calculi; 4 cases only of this series were exceptions to Courvoirsier's law. With the exception of these 4 cases which constituted only 5 per cent. of the total number examined every record of the Massachusetts General Hospital series in which definite statements are to be found concerning the points at issue goes to confirm Courvoirsier's law."

Peptic ulcer is a distinct organic ulceration of the gastroduodenal portion of the gut tube, and within its type the symptoms are constant and, as a rule, characteristic. Variations in symptomatology depend to a considerable extent upon the localization, since 70 per cent. of all peptic ulcers are located so as to interfere with the emptying power of the stomach. In the diagnosis the history is all important. Palpation, percussion and auscultation give evidence of very limited value; chemical examination of gastric contents give some confirmatory value only. The presence of gastric blood will be absent in over 75 per cent. of cases while roentgen-ray examination is positive in 67 to 80 per cent. of cases of duodenal and gastric ulcer respectively. With clinical methods alone we are able to make a correct diagnosis in 80 per cent. of cases. Three facts stand out in the history of all regular cases of peptic ulcer: (1) Pain; (2) time relation of pain to food ingestion; (3) periodicity of attacks.[18]

In all true ulcers in their symptom-producing stage a given set of symptoms are present or are introduced by certain articles of food or have a certain time interval in relation to the ingestion of food. These symptoms are constant and the interval or period is definite. If beefsteak produces pain upon ingestion then beefsteak during the symptom-producing stage always produces pain quite distinct and characteristic from the neuroses which intermit in their relationship from day to day. In ulcer if the pain is produced one hour after the ingestion of meat that interval is usually constant for the type of ulcer. Now, biologically in the beginning an ulcer manifests itself by irritations of the functions of the stomach and there is the interference or an irritation in the secretory motor functions, and there is the clinical condition of hyperchlorhydria from increased secretion or qualitative changes in acidity, and in the beginning there is usually hypertonus, hyperperistalsis and hypermotility.

The ingestion of food under normal circumstances is accompanied by a reflex process which is not perceived—a subconscious reflex—and when pain arises from the ingestion of food it points to an irritable process of the cord through which these reflexes pass as a result of oft-repeated painful stimuli. The epigastric region is essentially the place to which sensory symptoms are referred and the upper part of the left rectus muscle usually contracts first in response to an irritation from the stomach.[27]

A long history of gastric trouble associated with pain in the lower part of the epigastrium would suggest pyloric stenosis. We may therefore say that the patient with a gastro-duodenal ulcer presents in the main a history characterized by (1) pain, bearing some relation to the ingestion of food and the quality of food; (2) a chronicity; (3) the periodicity or the repetition of symptoms day after day during the symptom-producing period of the ulcer. As a corollary to these three are certain variant characters for certain types of ulcer; the nocturnal pain of duodenal ulcer and its rather specific type of hunger pain. Pain in ulcer follows the ingestion of food after a definite interval which is marked by the order and precision of its occurrence and its persistent occurrence throughout the whole history of the case.[21]

The complex of chronicity and the periodicity of attacks with pain or distress, repeated uniformly day by day during the attack and bearing a fairly definite relation to food intake and control is of primary clinical importance to the diagnosis of 80 per cent. of cases of uncomplicated peptic ulcer. In the remaining 20 per cent. this complex may be irregular, atypical or almost entirely absent, or the symptoms may be mixed, owing to coincidence of disease of contiguous organs which occurs in about 20 per cent. of all cases of ulcer.[19] In the irregular or atypical 20 per cent. the roentgen-ray examination with a bariumized carbohydrate meal is of great value: (1) By deformities of luminal contour; (2) by the triad of hypers—hypertonus, hyperperistalsis and hypermotility,[20] and of lessened value the determination of aberrations in gastric chemistry.

If an ulcer is situated on the lesser curvature near the cardiac end the symptoms are different than when located at the pylorus or in the duodenum. The symptoms of ulcer near the cardiac end will be those of pain, shortly after eating, with periodicity in its production, with the vomiting of partly digested food, with blood in the vomitus, with a progressive emaciation because the patient does not retain his food. With ulcers involving the pylorus there is soon introduced relative pyloric stenosis from spasm and secondary absolute pyloric stenosis from infiltration and spasm and the symptom of pain after the ingestion of food, when this interval gives place to the vomiting of large quantities of fermented material with food remnants. In the pyloric type of ulcer there is, as a rule, a loss of weight and secondarily a cachexia from absorption of fermented and putrefying gastric content. Now, quite distinct from these two types is that of the duodenal ulcer where the patient is, as a rule, well nourished and when he has food in his stomach is without distress.

Turning to duodenal ulcer, specifically we are in full accord with Moynihan that "persistent recurrent hyperchlorhydria is duodenal ulcer."[21] In gall-bladder disease, pain and discomfort usually come on with eating, while in duodenal ulcer the pain is relieved by eating. In duodenal ulcer the food that gives pain in pyloric ulcer gives relief in duodenal ulcer. The patient with duodenal ulcer, usually a man, is ordinarily a well-nourished individual, with marked appetency for food and who informs you that if he could eat all of the time he never would have a bit of pain. Consider his daily history: He starts out in the morning, eats a good breakfast and about 11 o'clock gets a pain, a pain that is usually described as gnawing, persistent and rather severe, but one that is tolerated. He seldom requires anodynes. He eats a sandwich or drinks a glass of milk and the pain disappears. The pain usually comes on when his stomach is empty and at about the time that he is naturally hungry. For this reason it becomes known as hunger pain. At about 4 o'clock the pain recurs and he takes another light lunch with rapid cessation of pain. Returning home he eats a well-proportioned supper, and before going to bed has a few crackers and a glass of milk. Sometimes about 12 o'clock he is awakened by epigastric pain of the previous type, but rather more severe. Repeated experience with the night pain has made it necessary to have some crackers or a piece of chocolate at his bedside. Upon eating something or taking soda the pain disappears. This history is repeated day after day with unvarying precision and consistency. Its story is typical and the diagnosis might be made as Moynihan expresses it "by correspondence."

The value of test meals is of confirmatory value only. In order of importance are: (1) food remnants, (2) blood, (3) acidity of test meal.[26]

In considering cancer of the stomach one may say that it makes its presence known only when ulceration occurs or when there is an interference with motor function of the stomach. The history is of most value in suggesting or arousing the suspicion of malignancy. There is, however, no isolated or significant sign or symptom upon which the diagnosis of early cancer can be predicated. The diagnosis of early cancer depends upon the mechanical interference produced, and it is an accident if the location of the growth is such as to introduce early the element of stenosis. If there is any symptom which stands out as between ulcer and cancer it is the known presence of periodicity of symptoms in ulcer and its absence in cancer. Periodicity is present in about 85 per cent. of ulcers and is absent in 99 per cent. of cases when that ulcer becomes malignant.[22]

Cancer of the stomach occurs in three forms: (1) The man who is perfectly well, who has an athletic stomach and who has never had any previous gastric distress. There comes into his history an abrupt sudden development of gastric signs. His symptoms suggest an acute ulcer of the stomach, with hemorrhage, but at the end of three or four weeks the man has lost physically beyond what would be expected of a simple ulcer. His anemia has become more pronounced, with a distaste or aversion for food, and finally from the anemia, emaciation and beginning cachexia the diagnosis of rapidly growing carcinoma is made. This type constitutes about 30 per cent. of all cancer cases and has an average duration of eight to ten months. The second class, and by far the largest proportion of about 60 per cent., is represented by the patient who has a perfectly clear history of chronic gastric ulcer extending over a period of years. A form of gastric distress characterized by periodic discomfort or pain usually bearing a distinct relationship to food ingestion with some vomiting. His previous gastric history covers a period of eight to ten years, with intermittent attacks of typical ulcer history. Finally, there comes an attack from which he does not respond to the medical treatment that heretofore has proved beneficial. The pain becomes constant, marked distaste for food intervenes with particular aversion to meat; blood is constantly present in the stool and vomitus and he has an average duration of cancer symptoms approximating six months. The third class, of about 10 per cent., is represented by the patient who has a typical history of gastric trouble from which he nearly but never quite recovers, and after a variable period progressively, but very slowly, becomes worse, with a distinct distaste for food and without any interruption progresses to a well-defined cachectic condition of malignancy.

No paper on affections of the right upper quadrant would be complete without considering chronic appendicitis. The commonest site of a "gastric ulcer" is the right ileac fossa.[21] In my personal experience at least 18 per cent. of cases coming to laparotomy have two lesions, either one of which offers an operative indication.

"Appendix dyspepsia" is a varied and indistinct clinical picture. It is usually more difficult to diagnose than either the conditions of ulcer or disease of the gall-bladder. If one can eliminate either of the two conditions named above it would be possible to arrive at a diagnosis of appendicular dyspepsia by elimination. In the ordinary case there is usually an absence of a history of an acute attack. Epigastric distress is a constant annoyance or sense of ache and usually with no distinct relationship to food. The pain or distress is apt to be aggravated by activity and motion and is occasionally relieved by an enema or a cathartic. It is infrequent for appendicular dyspepsia to be associated with a history of acute attacks, although occasionally local appendiceal pain may be elicited.

The chronically diseased appendix induces reflex gastric disturbances and usually contains fecaliths. The mechanism of disease is probably in a large majority of cases a pylorospasm with pain, vomiting, increased secretion, increased acidity, gaseous and sour eructations. It is noteworthy that the pain and distress is usually more prolonged than similar occurrences in disease of the gall-bladder. The distress is usually associated low down in the epigastrium or about the navel and lacks the distinct characters of localization as in biliary disease.

The outstanding features in the genesis of appendicular dyspepsia are its irregularity, variability and almost entire lack of periodicity. Food that at one period is associated with gastric irritability is upon another occasion eaten with zest and no distress. The attacks are distinctly less regular in their symptomatology than in ulcer.

It is interesting to note that McCarty[28] reported 59 cases when both the gall-bladder and appendix were removed and that 69 per cent. of the appendices showed distinct pathological changes. The ordinary postmortem incident of disease of the appendix is approximately 17 per cent.[25] Furthermore, in operations for cholecystitis 52 per cent. were associated with disease of the appendix, and in cholelithiasis 44 per cent. had distinct pathological changes in the appendix.

Paterson[23] found appendicular disease in association with gastric ulcer in 54 per cent. of cases and with duodenal ulcer in 66 per cent. of cases. Hutchinson[24] records 24 cases of fatal hemorrhage from the stomach after operations of various kinds upon the abdominal viscera. Of these 24, 21 were cases of appendicitis with septic complications. I have records of 4 cases of pronounced gastric hemorrhage which on very extensive abdominal exploration revealed no morbid process except in the appendix, and following an appendectomy there was a cessation of gastric distress and gastric hemorrhage.

Gastric hemorrhage has been experimentally produced by Rogers by injecting chemical irritants into the cecum and ascending colon, while irritation of the colon, *per se*, has been shown to bring about a gastric stasis and the delayed passage of food material through the small intestine.[29]

Barclay[30] quite recently has drawn attention to the spasmodic closure of the pylorus following reflex stimulation from the terminal ileum, when there is a too rapid overloading of the small intestine with chyme. Biologically the ileocecal valve represents a great point of chemical and bacterial partition, for at the cecum we have a change in chemical reaction; maximum bacterial flora, maximum fluidity, anastalsis, predominant lymphoid tissue and a point of natural or normal stasis.[31] These observations would seem to offer proof of a very extensive system of intra-alimentary reflexes acting upon the pyloric mechanism, and it would serve to explain the incidence of appendicular dyspepsia.

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ROENTGEN RAYS AS AN AID IN THE DIAGNOSIS OF ULCUS VENTRICULI.

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WHEN Cannon visualized the stomach in the animal by feeding it on food mixed with bismuth subnitrate, and Rieder introduced the bismuth meal for the same purpose in the human being, it was hoped that ulcer and cancer of the stomach would be absolutely accessible to diagnosis. While such hope was realized to a fair extent it cannot be too strongly emphasized that in the great majority of cases, especially of ulcer of the stomach, roentgen rays alone without the other clinical methods may quite often be misleading.

Roentgen-ray diagnosis of the diseases of the gastro-intestinal tract in general, and of ulcer of the stomach in particular, owes its development primarily to the Continental workers, notably among whom are to be mentioned Rieder, Holzknecht, Faulhaber, Kreuzfuchs, von Bergmann, Levy-Dorn, Barclay, and Hertz. Not long afterward the Americans began their very painstaking work, and here rank the names of Case, Carman, Pfahler, Jordan, Skinner,